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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/718,989
Filing Date: November 21, 2003
Appellant(s): SONG, XUEDONG

Jason W. Johnston
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed July 14, 2008 appealing from the Office action mailed December 12, 2007.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

US 2002/0004246	DANIELS et al.	1-2002
US 6,770,220	KLIMANT	8-2004
US 5,674,698	ZARLING et al.	10-1997
WO 97/09620	RYLATT et al.	3-1997
US 5,670,381	JOU et al.	9-1997

O'Riordan et al. "Monofunctional Derivatives of Coproporphyrins for Phosphorescent Labeling of Proteins and Binding Assays," Anal. Biochem. vol 290, (2001), pp366-375.

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 64 – 77, 79, 80, and 82 – 84 are rejected under 35 U.S.C. 103(a) as being unpatentable over Daniels et al. (US 2002/0004246) in view of Klimant (US 6,770,220), and in light of O'Riordan et al. ("Monofunctional Derivatives of Coproporphyins for Phosphorescent Labeling of Proteins and Binding Assays," *Anal. Biochem.* **290** (2001) 366-375).

Daniels et al. teach a method for detecting an analyte within a test sample, the method comprising:

i) providing a lateral flow test strip (assay device) that comprises a porous membrane in fluid communication with semiconductor nanocrystals (luminescent or phosphorescent particles) conjugated with a specific binding member, wherein the porous membrane defines a capture region (detection zone) within which is immobilized a capture reagent;

ii) contacting the lateral flow test strip with the test sample;

iii) subjecting the capture region to illumination to generate a detection signal; and

iv) thereafter, measuring the intensity of the detection signal, wherein the amount of the analyte within the test sample is proportional to the intensity of the detection signal (see Figure 1; and paragraphs [0016]-[0028], [0079]-[0082], [0095], [0109], [0111], [0115]-[0120], [0126]-[0128], [0170], and [0212]-[0215]).

However, Daniels et al. fail to teach that the luminescent/phosphorescent particle comprises a phosphorescent label encapsulated within a matrix and that the label has an emission lifetime of about 1 microsecond or more and a Stokes shift of greater than about 100 nanometers.

Klimant teaches of the production and use of luminescent microparticles wherein long-lived phosphorescent labels are incorporated (encapsulated) within solid particles for use as internal standards for referencing phosphorescence signals or as markers for labeling and detecting biomolecules (see column 1, lines 1-16). Luminescence measurements using phosphorescence signals is a very common method in biological and chemical analysis dues to its high sensitivity and versatility (see column 1, lines 30-35). The incorporation of the phosphorescence labels within matrices allows for elimination or great reduction in phosphorescence signal quenching by interfering oxygen that is common during luminescence measurement (see column 1, lines 17-23).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine with the detection method of Daniels et al. the luminescent microparticles taught by Klimant because Klimant teaches the benefit of luminescent microparticles that comprise phosphorescence labels encapsulated within matrices because the microparticles create long-lived luminescence, wherein the matrices eliminate or greatly reduce phosphorescence signal quenching by interfering oxygen that is common during luminescence measurement.

With respect to Applicant's limitations in claim 64 requiring the phosphorescent labels to have an emission lifetime of about 1 microsecond or more and a Stokes shift of

100 nm or more, the phosphorescent labels used by Klimant preferably comprise metal/ligand complexes that include porphyin complexes of Pt(II) or Pd(II), which are known in the art to have emission lifetimes of 1 microsecond or more and Stokes shift of 100 nm or more (see Klimant: column 3, lines 14-36; and O'Riordan et al.: p366).

With respect to Applicant's claims 65, 66, and 68, Klimant teaches that the phosphorescent label is a metal/ligand complex, particularly comprised of transition metals such as ruthenium, osmium, iridium, rhenium, platinum, or palladium, and also containing complex ligands, such as **bipyridine**, bipyrazine, phenanthroline, terpyridil or derivatives thereof (see column 3, lines 14-21).

With respect to Applicant's claims 67 and 69, Klimant teaches the phosphorescent label can further comprise a porphyrin ligand or porphyrin complex with platinum(II) or palladium(II), which anticipates Applicant's claims 7 and 31 because the porphyin complexes encompass the derivatives and combinations thereof and are being utilized for the same purpose (see column 3, lines 25-31).

With respect to Applicant's claim 70, Klimant teaches the matrix incorporating the phosphorescent label comprises polymer particles (see column 4, lines 11-19).

With respect to Applicant's claims 71 and 72, Klimant teaches the size of the luminescent particles in the range of 20 µm to 10 µm, particularly from 50 nm to 1 µm (see column 3, lines 37-39).

With respect to Applicant's claim 73, Klimant teaches the matrix incorporating the phosphorescent label protects the label from quenching (see column 1, lines 17-23).

With respect to Applicant's claims 74 and 75, Klimant teaches the matrix incorporating the phosphorescent label protects the label from quenching, enabling the luminescence lifetime (detection signal) to be only 20%, at most 15% and preferably at most 10% shorter than in an O_2 free environment, which anticipates Applicant's claims 74 and 75 (see column 3, lines 5-13).

With respect to Applicant's claims 76 and 77, the phosphorescent labels used by Klimant preferably comprise metal/ligand complexes that include porphyin complexes of Pt(II) or Pd(II), which are known in the art to have emission lifetimes of up to 1000 microseconds (see Klimant: column 3, lines 14-36; and O'Riordan et al.: p366).

With respect to Applicant's claim 79, Daniels et al. teach that the capture reagent in the capture region comprises a specific binding member, such as an antigen, hapten, antibody, or streptavidin (see Figures 1 and 2; and paragraphs [0025], [0088]-[0090], and [0116]).

With respect to Applicant's claim 80, Daniels et al. teach that the illumination source can be a pulsed excitation source (see paragraph [0170]).

With respect to Applicant's claims 82-84, Daniels et al. teach that the specific binding member that is conjugated to the luminescent particles, i.e. semiconductor nanocrystals, is configured to preferentially bind with the analyte and can comprise antigens, haptens, aptamers, and antibodies, as well as analogs of the analyte itself (see paragraphs [0016], [0024], [0088]-[0090], and [0094]-[0098]).

Claims 78 and 81 are rejected under 35 U.S.C. 103(a) as being unpatentable over Daniels et al. (US 2002/0004246) in view of Klimant (US 6,770,220), as applied to claim 64 above, and further in view of Zarling et al. (US 5,674,698).

The Daniels et al. and Klimant references, which were discussed in the 103(a) rejection above, fail to teach that the detection signal is measured from 1 to 100 microseconds after the detection zone is subjected to one or more pulses of illumination, or that the signal is measured by a time-gated detector.

Zarling et al. teach of up-converting and down-converting phosphorescent/luminescent reporters for use in biological assays using laser excitation techniques. The detection and quantitation of the phosphorescent reporters is accomplished by illuminating the sample suspected of containing the reporters and detecting the phosphorescent radiation at more or more emission bands. Various means can be used for detection of the phosphorescent emission(s), including a time-gated and/or frequency-gated light detector for rejection of residual background noise. Time-gated detection is desirable because it provides a method of recording long-lived emission after termination of illumination, wherein signal(s) attributable to phosphorescence is recorded, while short-lived autofluorescence and scattered illumination light is rejected. A pulsed excitation source is preferable for use with a time-gated detector, wherein the phosphorescent reporters have emission lifetimes on the order of 1 ms (see Abstract; column 1, lines 12-18; column 31, lines 50-56; column 32, lines 54-67; and column 33, lines 1-18).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to include with the detection method of Daniels et al. and Klimant the use of a pulsed excitation source and time-gated detection, wherein the detection signal is measured a certain time period after the excitation as taught by Zarling et al. because Zarling et al. teach the advantages of using a pulsed excitation source and time-gated detection with phosphorescent labels because it provides a method of recording long-lived emission after termination of illumination, wherein signal(s) attributable to phosphorescence is recorded, while short-lived autofluorescence and scattered illumination light is rejected.

Claims 85 and 89 – 91 are rejected under 35 U.S.C. 103(a) as being unpatentable over Daniels et al. (US 2002/0004246) in view of Klimant (US 6,770,220), as applied to claim 64 above, and further in view of Rylatt et al. (WO 97/009620).

Daniels et al. teach an additional control line or region, but fail to teach that the control line works as a calibration zone, wherein the intensity of the detection signal is calibrated by the intensity of the calibration signal. Klimant also fails to teach the use of a calibration zone.

Rylatt et al. teach a method for quantitative determination of a target analyte in a test sample, comprising a lateral flow assay device wherein a liquid permeable membrane (porous membrane) is used, wherein said membrane contains a test zone (detection zone) and at least one calibration zone(s) (see p4, lines 29-30 and p5, lines 1-20). The membrane also utilizes an analyte detection agent (detection probe)

comprising a specific binding partner and an associated label (see p7, lines 25-29 in particular). The test zone (detection zone) utilizes an immobilized analyte receptor (capture reagent) that can bind with the analyte and/or analyte detection agent (detection probe) and generate a detectable signal. The calibration zone includes an immobilized calibration agent receptor that binds to the specific binding partner found on the analyte detection agent (detection probe) or calibration agent (calibration probe) and further, the binding of the agent to the calibration zone produces a calibration signal that is used to calibrate the signal produced in the test zone (detection signal) (see p5, lines 10-20 and p9, lines 13-19 in particular). Therefore, the lateral flow membrane, containing the analyte detection agent (detection probes), is contacted with the test sample; the analyte detection agent (detection probes) binds to the target analyte and flows to the test zone (detection zone) wherein it binds to an immobilized analyte receptor, and generates a signal, which is detected and measured, thus providing the amount of analyte in the test sample, which is proportional to the intensity of the signal at the test zone (detection signal) calibrated by the intensity of the calibration signal (see p18-20 in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to include with the detection method of Daniels et al. and Klimant a calibration zone as taught by Rylatt et al. because Rylatt et al. teach the benefit of including a calibration zone with a test zone on a lateral flow assay device in order to provide accurate quantitative determination of a target analyte in a test sample,

because the signal produced in the calibration zone is utilized to calibrate the signal produced in the test zone.

Claim 92 is rejected under 35 U.S.C. 103(a) as being unpatentable over Daniels et al. (US 2002/0004246) in view of Klimant (US 6,770,220) and Rylatt et al. (WO 97/009620), as applied to claim 85 above, and further in view of Jou et al. (US 5,670,381).

The Daniels et al., Klimant, and Rylatt et al. references discussed above fail to teach that the capture reagent included in the calibration zone comprises a polyelectrolyte.

Jou et al. teach a device for performing an assay comprising a porous material containing a capture or reaction zone with an immobilized capture reagent. The device utilizes a specific binding member attached to a charged substance that is contacted with an analyte of interest to form a complex. The complex binds to the immobilized capture reagent in the capture or reaction zone through ion-capture, wherein the capture reagent is oppositely charged with respect to the charged substance of the analyte complex. The capture reagent preferably comprises an anionic or cationic polymeric substance (polyelectrolyte), which enables the production of a generic solid phase device for use in specific binding assays. Assay procedures for many different analytes can use the same solid phase material which contains a predetermined zone of anionic or cationic capture polymer rather than an immobilized binding member capable of binding only a specific analyte as found in conventional flow-through or test-

strip devices. Further, the ion-capture technique increases the potential number of complexes that can be immobilized on the solid support (see column 6, lines 25-40; column 7, lines 1-46; column 10, lines 63-65; column 19, lines 29-67; column 22, lines 29-67; and column 23, lines 1-26).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to include with the detection method of Daniels et al., Klimant and Rylatt et al. a polyelectrolyte as the capture reagent in the control region (calibration zone) as taught by Jou et al. because Jou et al. teach the benefit of using an anionic or cationic polymeric substance as the immobilized capture reagent in a capture zone because the polymeric substance allows for the binding of a conjugated substance or complex to a solid phase support material through ion-capture, which increases the potential number of complexes that can be immobilized on the solid support and allows for the production of a generic solid phase device, wherein many different analytes can use the same solid phase material which contains a predetermined zone of anionic or cationic capture polymer rather than an immobilized binding member capable of binding only a specific analyte as found in conventional flow-through or test-strip devices.

(10) Response to Argument

Applicant's arguments have been fully considered but they are not persuasive.

I. Applicant's first argument (see pages 4-17 of Appeal Brief) is with regard to the rejection of claims 64-77, 79, 80 and 82-84 under 35 U.S.C. 103(a) as being unpatentable over Daniels et al. (US 2002/0004246) in view of Klimant (US

6,770,220), and in light of O'Riordan et al. ("Monofunctional Derivatives of Coproporphyins for Phosphorescent Labeling of Proteins and Binding Assays," *Anal. Biochem.* **290** (2001) 366-375). In particular, Applicant argues that a *prima facie* case of obviousness has not been established for modifying the teachings of Daniels et al. according to the teachings of Klimant in light of O'Riordan et al. in order to arrive at Applicant's instant claims because:

(1) The semiconductor nanocrystals of Daniels et al. are not functionally equivalent to the luminescent particles of Klimant;

(2) The references teach away from the suggested combination;

(3) The proposed modification of Daniels et al. would render the invention of Daniels et al. unsatisfactory for its intended purpose; and

(4) Only improper hindsight would lead the person of ordinary skill from Daniels et al., Klimant, and O'Riordan et al. to the limitations of Applicant's instant claims.

However, these arguments are not found persuasive.

Before discussing the particular arguments of Applicant, the reasons behind the combination of Daniels et al. in view of Klimant will be discussed. The primary reference of Daniels et al. teaches a similar device and method of use according to Applicant's instant claims, wherein the method of Daniels et al. comprises:

i) providing a lateral flow test strip (assay device) that comprises a porous membrane in fluid communication with semiconductor nanocrystals (luminescent or phosphorescent particles) conjugated with a specific binding member, wherein the

porous membrane defines a capture region (detection zone) within which is immobilized a capture reagent;

ii) contacting the lateral flow test strip with the test sample;

iii) subjecting the capture region to illumination to generate a detection signal; and

iv) thereafter, measuring the intensity of the detection signal, wherein the amount of the analyte within the test sample is proportional to the intensity of the detection signal (see Figure 1; and paragraphs [0016]-[0028], [0079]-[0082], [0095], [0109], [0111], [0115]-[0120], [0126]-[0128], [0170], and [0212]-[0215]).

However, Daniels et al. fail to teach that the luminescent/phosphorescent particle comprises a phosphorescent label encapsulated within a matrix and that the label has an emission lifetime of about 1 microsecond or more and a Stokes shift of greater than about 100 nanometers. Therefore, the secondary reference of Klimant was combined with Daniels et al. in order to provide a teaching of and motivation for substituting the luminescent/phosphorescent particles of Klimant, which comprise a phosphorescent label encapsulated within a matrix, with the semiconductor labels of Daniels et al. In particular, Klimant teaches of the production and use of luminescent microparticles wherein long-lived phosphorescent labels are incorporated (encapsulated) within solid particles for use as internal standards for referencing phosphorescence signals or as markers for labeling and detecting biomolecules (see column 1, lines 1-16). Luminescence measurements using phosphorescence signals is a very common method in biological and chemical analysis dues to its high sensitivity and versatility

(see column 1, lines 30-35). The incorporation of the phosphorescence labels within matrices allows for elimination or great reduction in phosphorescence signal quenching by interfering oxygen that is common during luminescence measurement (see column 1, lines 17-23).

Therefore, it was determined that it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine with the detection method of Daniels et al. the luminescent microparticles taught by Klimant because Klimant teaches the benefit of luminescent microparticles that comprise phosphorescence labels encapsulated within matrices because the microparticles create long-lived luminescence, wherein the matrices eliminate or greatly reduce phosphorescence signal quenching by interfering oxygen that is common during luminescence measurement.

The third or evidentiary reference of O'Riordan et al. was merely combined with the combination of Daniels et al. in view of Klimant in order to provide evidence that the luminescent/phosphorescent labels taught by Klimant, which preferably comprise metal/ligand complexes that include porphyin complexes of Pt(II) or Pd(II), would have an emission lifetime of about 1 microsecond or more and a Stokes shift of 100 nm or more as known in the art (see Klimant: column 3, lines 14-36; and O'Riordan et al.: p366).

(1) The semiconductor nanocrystals of Daniels et al. are not functionally equivalent to the luminescent particles of Klimant.

With respect to Applicant's first argument over the non-equivalence of the semiconductor nanocrystals of Daniels et al. and the luminescent particles of Klimant, the semiconductor nanocrystals of Daniels et al., which represent luminescent particles, would be considered functionally equivalent to the luminescent particles of Klimant because both particles provide detectable luminescent/phosphorescent signals when excited by an excitation source, can be conjugated to biomolecules, and can be effectively used as markers for labeling and detecting biomolecules (see paragraphs [0024], [0027], [0028], [0079] and [0082] of Daniels et al.; and column 1, lines 4-16; column 2, lines 51-60; and column 5, lines 23-52 of Klimant). Further, the evidence provided in both the Daniels et al. and Klimant references, which is presented directly above, and in the previous final rejection, provides the reasoning behind the functional equivalence of the labels used by these two references and thus, Examiner did not go on official notice but did in fact provide supporting documentary evidence.

In addition, Applicant argues over the "types of luminescent signals" created by the semiconductor particles of Daniels et al. as compared to the particles taught by Klimant (see pages 9-11 of Appeal Brief). These arguments are not considered persuasive or relevant because both particles fall within the family of luminescent labels used as markers for labeling and detecting biomolecules (see paragraphs [0079] and [0082] of Daniels et al; and column 1, lines 4-16; column 2, lines 51-60; and column 5, lines 23-52 of Klimant). Therefore, the materials used to create the particle labels, their different detection techniques, and their different characteristics, which relates to their methods of production and detection, are not considered relevant because the

subsitution of the phosphorescent particles taught by Klimant in the immunochromatographic method of Daniels et al. would provide an effective means for labeling and detecting biomolecules via luminescence given that Klimant provides teaching that their phosphorescent labels can be utilized as markers for labeling and detecting biomolecules and there is no suggestion that the use of the phosphorescent particles in the system of Daniels et al. would be inoperative.

(2) The references teach away from the suggested combination.

With respect to Applicant's second argument that the references teach away from the suggested combination, as discussed above, the Klimant reference provides a teaching of and motivation for substituting the luminescent/phosphorescent particles of Klimant with the semiconductor particles of Daniels et al. because Klimant teaches the benefit of luminescent microparticles that comprise phosphorescence labels encapsulated within matrices given that the microparticles create long-lived luminescence, wherein the matrices eliminate or greatly reduce phosphorescence signal quenching by interfering oxygen that is common during luminescence measurement. The specific characteristics and detection schemes taught by Daniels et al. for their semiconductor nanocrystals provides teaching on how to prepare and detect their luminescent labels. However, the luminescent labels of Daniels et al. are **not** being relied upon in the method created by the combination of Daniels et al. in view of Klimant. Therefore, the characteristics and detection techniques of Daniels et al. do not teach away from the use of the luminescent/phosphorescent particles of Klimant, but

merely provide the means to prepare and detect semiconductor particles when used in their method of labeling and detecting analytes. The beneficial aspects of the luminescent/phosphorescent particles taught by Klimant provide a reasoning behind and motivation for the substitution of these particles with the semiconductor particles of Daniels et al. and therefore, do not teach away from this combination.

In addition, Applicant appears to be arguing against the references individually, and one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

(3) The proposed modification of Daniels et al. would render the invention of Daniels et al. unsatisfactory for its intended purpose.

With respect to Applicant's third argument that the proposed modification of Daniels et al. would render their invention unsatisfactory, again, as discussed above, the specific characteristics and detection schemes taught by Daniels et al. for their semiconductor nanocrystals provides teaching on how to prepare and detect their luminescent labels. However, the luminescent labels of Daniels et al. are **not** being relied upon in the method created by the combination of Daniels et al. in view of Klimant. Therefore, the use of the luminescent/phosphorescent particles of Klimant in the method of Daniels et al. would not render the invention of Daniels et al. unsatisfactory given the beneficial aspects of the luminescent/phosphorescent particles

taught by Klimant, as well as the reasoning behind and motivation taught by Klimant for the substitution of these particles with the semiconductor particles of Daniels et al.

In addition, and as discussed above, Applicant appears to be arguing against the references individually, and one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

(4) Only improper hindsight would lead the person of ordinary skill from Daniels et al., Klimant, and O'Riordan et al. to the limitations of Applicant's instant claims.

With respect to Applicant's final argument over improper hindsight, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). The teachings of Daniels et al. in view of Klimant provide the knowledge that was within one of ordinary skill in the art at the time the invention was made and also provide the reasoning and motivation for this combination in order to render obvious Applicant's instant claims. Therefore, impermissible or improper hindsight was not relied upon in order to render obvious Applicant's instant claims.

II. Applicant's second argument (see pages 17-20 of Appeal Brief) is with regard to the rejection of claims 78 and 81 under 35 U.S.C. 103(a) as being unpatentable over Daniels et al. (US 2002/0004246) in view of Klimant (US 6,770,220), and further in view of Zarling et al. (US 5,674,698). In particular, Applicant argues:

(1) That one of ordinary skill in the art would not have looked to Zarling et al. for combination with Daniels et al. because the systems are extremely different with regard to their excitation requirements, the detection regimes, and the analysis techniques; and

(2) Only improper hindsight would lead the person of ordinary skill from Zarling et al, Daniels et al., and Klimant to the limitations of Applicant's instant claims.

However, these arguments are not found persuasive.

(1) That one of ordinary skill in the art would not have looked to Zarling et al. for combination with Daniels et al. because the systems are extremely different with regard to their excitation requirements, the detection regimes, and the analysis techniques.

With respect to Applicant's first argument, the Zarling et al. reference was combined with Daniels et al. and Klimant in order to provide a teaching of and motivation for utilizing a pulsed excitation source and time-gated detection with luminescent/phosphorescent labels, wherein the detection signal is measured a certain time period after the excitation as taught by Zarling et al. because Zarling et al. teach the advantages of using a pulsed excitation source and time-gated detection with phosphorescent labels because it provides a method of recording long-lived emission after termination of illumination, wherein signal(s) attributable to phosphorescence is

recorded, while short-lived autofluorescence and scattered illumination light is rejected (see Abstract; column 1, lines 12-18; column 31, lines 50-56; column 32, lines 54-67; and column 33, lines 1-18 of Zarling et al). Applicant is again arguing against the references individually, and one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Further, Applicant is comparing the luminescent materials, detection regimes, and analysis techniques of Zarling et al. primarily with the luminescent materials, detection regimes, and analysis techniques of Daniels et al. when the rejection is based on the method created by the combination of Daniels et al. in view of Klimant, wherein the semiconductor nanocrystals of Daniels et al. are being substituted with the luminescent particles of Klimant. In addition, the labels taught by Daniels et al. are **not** being relied upon in the combination created by Daniels et al. in view of Klimant, and thus, the comparison between the luminescent materials of Daniels et al. with those taught by Zarling et al. is considered irrelevant.

(2) Only improper hindsight would lead the person of ordinary skill from Zarling et al, Daniels et al., and Klimant to the limitations of Applicant's instant claims.

With respect to Applicant's second argument over improper hindsight, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made,

and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). The teachings of Daniels et al. in view of Klimant and Zarling et al. provide the knowledge that was within one of ordinary skill in the art at the time the invention was made and also provide the reasoning and motivation for this combination in order to render obvious Applicant's instant claims. Therefore, impermissible or improper hindsight was not relied upon in order to render obvious Applicant's instant claims.

III. Applicant's third argument (see page 20 of Appeal Brief) is with regard to the rejection of claims 85 and 89-91 under 35 U.S.C. 103(a) as being unpatentable over Daniels et al. (US 2002/0004246) in view of Klimant (US 6,770,220), and further in view of Rylatt et al. (WO 97/009620). In particular, Applicant argues that these claims depend from an allowable independent claim as discussed in their previous rejections presented in the Appeal Brief.

As discussed above, these arguments have not been considered persuasive. Therefore, the rejection of claims 85 and 89-91 under 35 U.S.C. 103(a) as being unpatentable over Daniels et al. in view of Klimant, and further in view of Rylatt et al. is maintained given that the independent claim from which these claims depend is not considered allowable.

IV. Applicant's fourth and final argument (see pages 20-26 of Appeal Brief) is with regard to the rejection of claim 92 under 35 U.S.C. 103(a) as being unpatentable

over Daniels et al. (US 2002/0004246) in view of Klimant (US 6,770,220) and Rylatt et al. (WO 97/009620), and further in view of Jou et al. (US 5,670,381). In particular, Applicant argues:

(1) The proposed modification of Daniels et al. would render the invention of Daniels et al. unsatisfactory for its intended purpose;

(2) The combination of Jou et al. with Daniels et al., Klimant and Rylatt et al. fails to teach or suggest limitations of claim 92; and

(3) Only improper hindsight would lead the person of ordinary skill from Jou et al, Rylatt et al., Daniels et al., and Klimant to the limitations of Applicant's claim 92.

(1) The proposed modification of Daniels et al. would render the invention of Daniels et al. unsatisfactory for its intended purpose.

With respect to Applicant's first argument that the modification of Daniels et al. would render unsatisfactory the invention of Daniels et al., the modification of the invention of Daniels et al. to include a calibration zone as taught by Rylatt et al. is considered obvious given the teaching of and motivation for a calibration zone as taught by Rylatt et al., wherein Rylatt et al. teach the benefit of including a calibration zone with a test zone on a lateral flow assay device in order to provide accurate quantitative determination of a target analyte in a test sample, because the signal produced in the calibration zone is utilized to calibrate the signal produced in the test zone (see p4, lines 29-30; p5, lines 1-20; p7, lines 25-29; p9, lines 13-19; and p18-20 of Rylatt et al.). The further modification of this calibration zone to comprise a polyelectrolyte as taught by

Jou et al. is considered obvious given the teaching of and motivation for the use of a polyelectrolyte in a binding region as taught by Jou et al., wherein Jou et al. teach the benefit of using an anionic or cationic polymeric substance (i.e. polyelectrolyte) as the immobilized capture reagent in a capture zone/binding region because the polymeric substance allows for the binding of a conjugated substance or complex to a solid phase support material through ion-capture, which increases the potential number of complexes that can be immobilized on the solid support and allows for the production of a generic solid phase device, wherein many different analytes can use the same solid phase material which contains a predetermined zone of anionic or cationic capture polymer rather than an immobilized binding member capable of binding only a specific analyte as found in conventional flow-through or test-strip devices (see column 6, lines 25-40; column 7, lines 1-46; column 10, lines 63-65; column 19, lines 29-67; column 22, lines 29-67; and column 23, lines 1-26 of Jou et al.). The charged polymeric substance or reagent bound to the membrane of Jou et al. at the capture or detection site coincides with and is substituted for the calibration agent receptor of Rylatt et al., wherein both of these substances bind to a provided assay reagent, wherein the assay reagent of Jou et al. is the charged substance/capture reagent that can bind to the charged substance bound to the membrane; and the assay reagent of Rylatt et al. is the calibration agent that can bind to the calibration agent receptor bound to the membrane (see column 24, lines 49-67; column 25, lines 1-67; column 26, lines 1-67; column 28, lines 1-67; and column 29, lines 1-10 of Jou et al; and p4, lines 29-30; p5, lines 1-20; p7, lines 25-29; p9, lines 13-19; and p18-20 of Rylatt et al). Therefore, the combination

of Daniels et al. in view of Klimant and Rylatt et al., and further in view of Jou et al. would result in the test strip of Daniels et al. containing a calibration zone as taught by Rylatt et al., wherein the calibration zone comprises a polyelectrolyte as taught by Jou et al. This modification would not render the invention of Daniels et al. unsatisfactory, but merely provide the benefits, as discussed above and as taught by the Rylatt et al. and Jou et al. references.

(2) The combination of Jou et al. with Daniels et al., Klimant and Rylatt et al. fails to teach or suggest limitations of claim 92.

With respect to Applicant's second argument that the combination of Jou et al. with Daniels et al., Klimant and Rylatt et al. fails to teach the limitation of claim 92, i.e. that the calibration capture reagent comprises a polyelectrolyte, as discussed above, the combination of Daniels et al. in view of Klimant and Rylatt et al., and further in view of Jou et al. would result in the test strip of Daniels et al. containing a calibration zone as taught by Rylatt et al., wherein the calibration zone comprises a polyelectrolyte as taught by Jou et al. Jou et al. provides a teaching of and motivation for utilizing a charged polymeric substance, i.e. polyelectrolyte, in a binding region, wherein Jou et al. teach the benefit of using an anionic or cationic polymeric substance as the immobilized capture reagent in a capture zone/binding region because the polymeric substance allows for the binding of a conjugated substance or complex to a solid phase support material through ion-capture, which increases the potential number of complexes that can be immobilized on the solid support and allows for the production of a generic solid

phase device, wherein many different analytes can use the same solid phase material which contains a predetermined zone of anionic or cationic capture polymer rather than an immobilized binding member capable of binding only a specific analyte as found in conventional flow-through or test-strip devices (see column 6, lines 25-40; column 7, lines 1-46; column 10, lines 63-65; column 19, lines 29-67; column 22, lines 29-67; and column 23, lines 1-26 of Jou et al.). The charged polymeric substance of Jou et al. does not necessarily only have to be utilized in a test zone or capture region, but in any region where a binding interaction is to occur between two, preferably charged, substances. Therefore, the combination of Jou et al. with Daniels et al., Klimant and Rylatt et al. does in fact teach the limitations of claim 92, because the charged substance (i.e. polyelectrolyte) of Jou et al. can be utilized in the calibration zone of Rylatt et al., which is provided on the device of Daniels et al. for the beneficial reasons discussed above.

(3) Only improper hindsight would lead the person of ordinary skill from Jou et al, Rylatt et al., Daniels et al., and Klimant to the limitations of Applicant's claim 92.

With respect to Applicant's final argument over improper hindsight, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA

1971). The teachings of Daniels et al. in view of Klimant, Rylatt et al. and Jou et al. provide the knowledge that was within one of ordinary skill in the art at the time the invention was made and also provide the reasoning and motivation for this combination in order to render obvious Applicant's instant claims. Therefore, impermissible or improper hindsight was not relied upon in order to render obvious Applicant's instant claims.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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